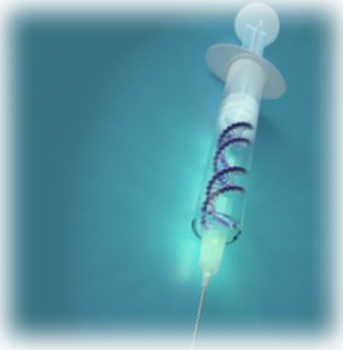
A paradigm shift and its implications for medcomms

Gene and cell therapies

Tim Mustill
Principal Consultant

MedComms Networking Brunch Club
Oct 4, 2017

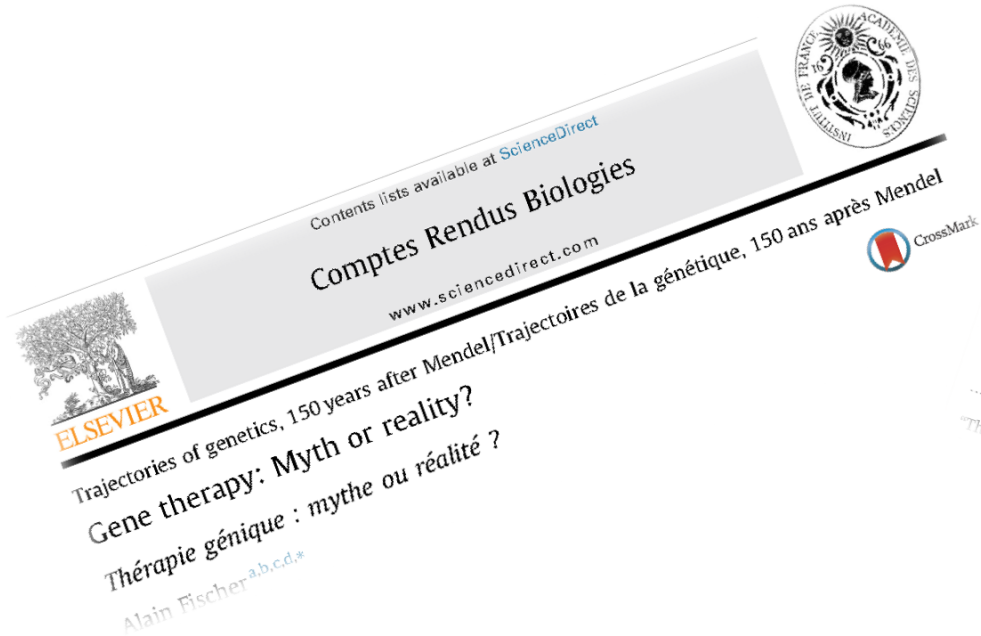


Agenda

- Gene and cell therapy primer
- Development pitfalls and therapeutic promise
- Challenges and opportunities for growth
- How can medcomms help?

Key questions

- Why is this such an exciting and dynamic field?
- What's taking so long?
- Why are advanced therapies so different?
- (How) can medcomms help?



Contents lists available at ScienceDirect

Comptes Rendus Biologies

www.sciencedirect.com

Trajectories of genetics, 150 years after Mendel/Trajectoires de la génétique, 150 ans après Mendel

Gene therapy: Myth or reality?

Thérapie génique : mythe ou réalité ?

Alain Fischer[a,b,c,d,*]

GENETIC LITERACY PROJECT

SCIENCE NOT IDEOLOGY

ABOUT HUMAN FOOD & AGRICULTURE SPECIAL SECTIONS RESOURCES

CRISPR's high costs may limit development of gene therapy drugs

Jim Kozubek | July 6, 2017 | STAT

The ruckus over the CRISPR gene-editing system hides a dark reality: its high cost may make it unaffordable and questions remain whether most insurance companies will pay for it....

"The cost isn't coming

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Jim Kozubek

- Life hacking: Gene editing won't solve all of society's problems
- Is the Broad Institute exploiting its nonprofit status to corner CRISPR business?
- What role should society play in decisions about gene

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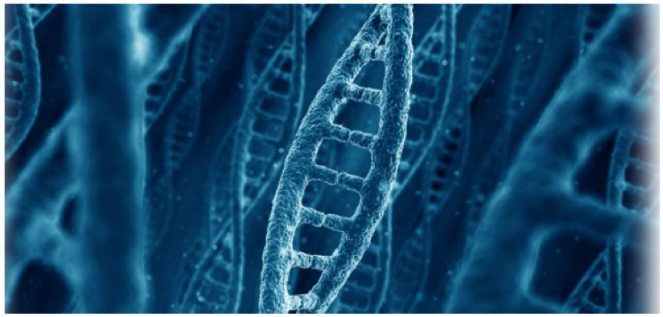
Opinion

VIEWPOINT

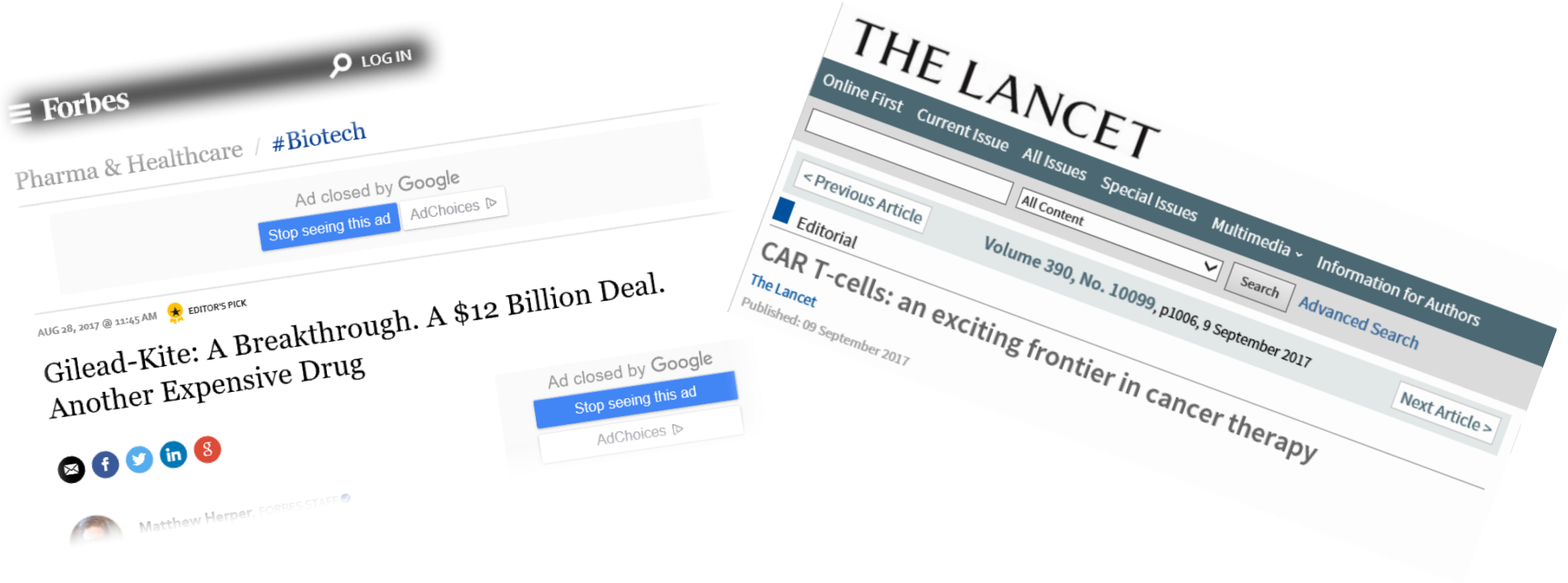
What Happens When Underperforming Big Ideas in Research Become Entrenched?



FEATURE

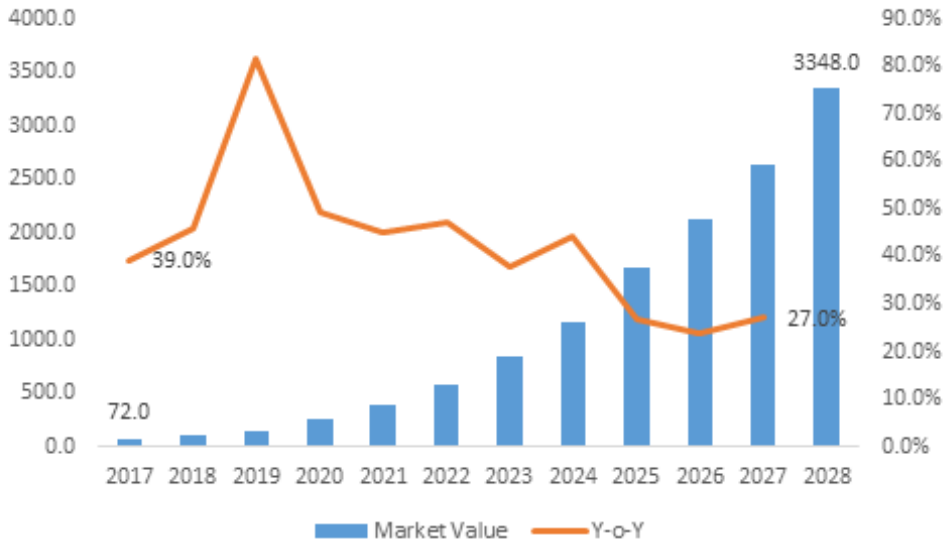
A new wave of gene therapies ready to hit US shores

On a more positive note



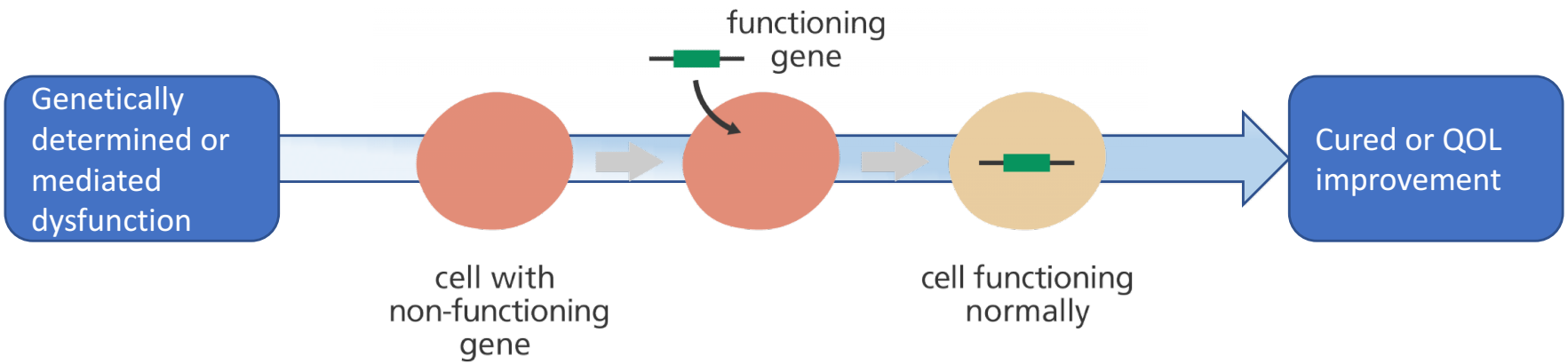
Why is it interesting and exciting?

Figure 1. North America CAR T Cell Therapy Market Size and Forecast, US$ Million and Y-o-Y Growth (%)

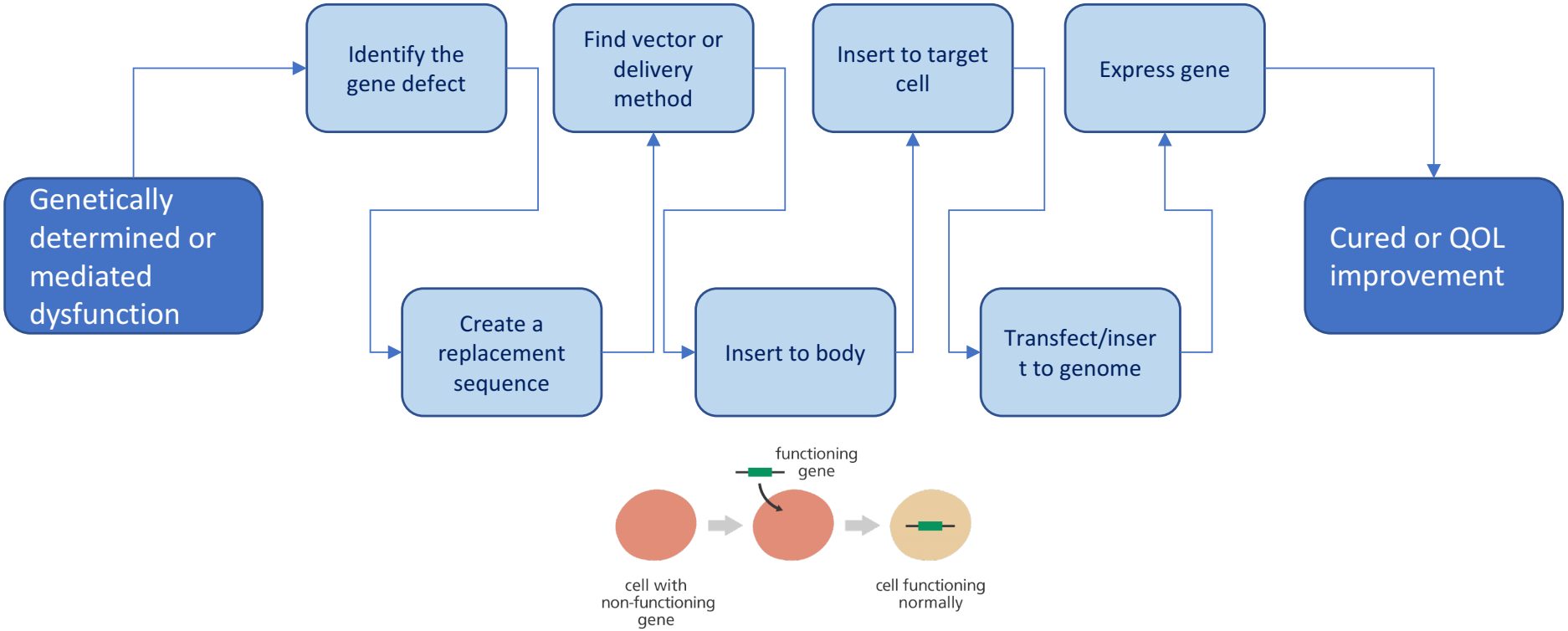


Source: Coherent Market Insights Analysis (2017)

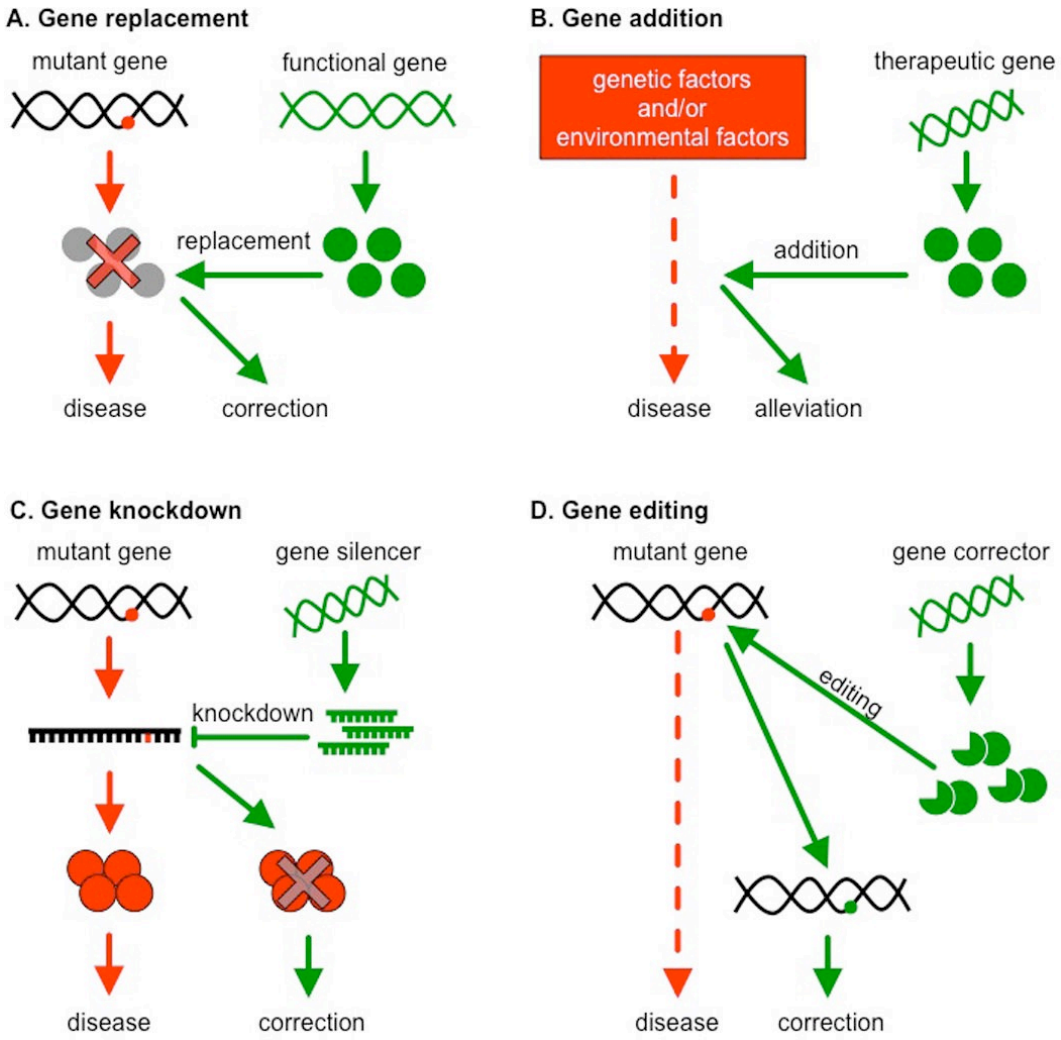
Simple concept!



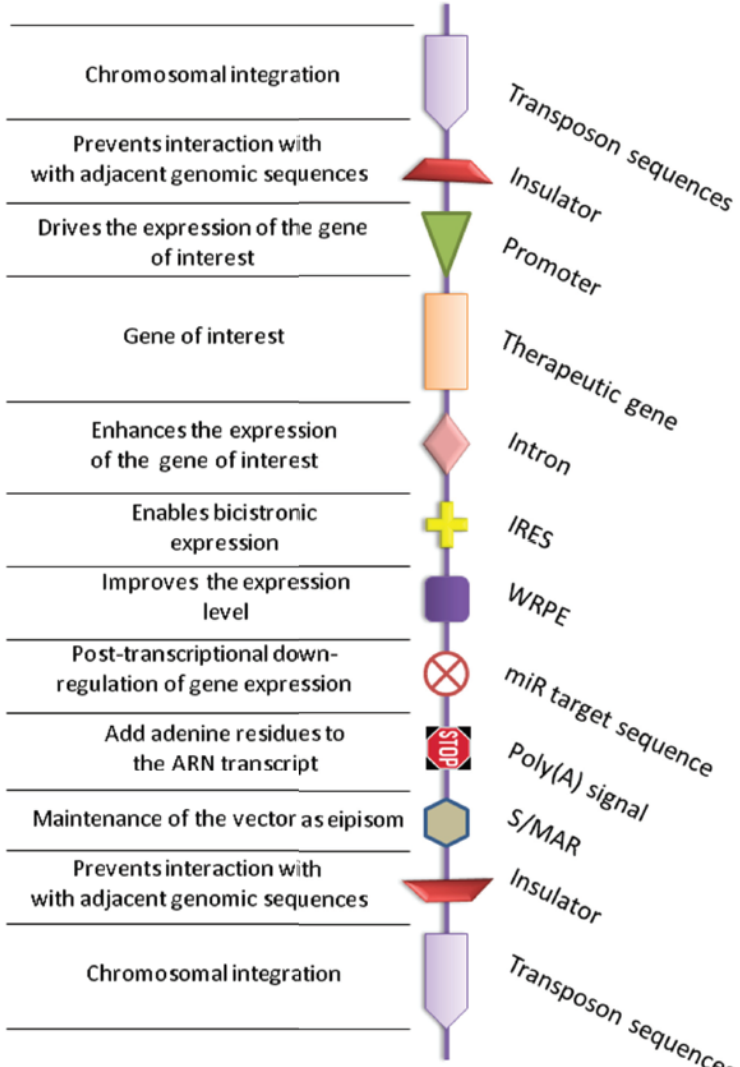
Breaking out the 3 step process



Main strategies



Gene expression cassette

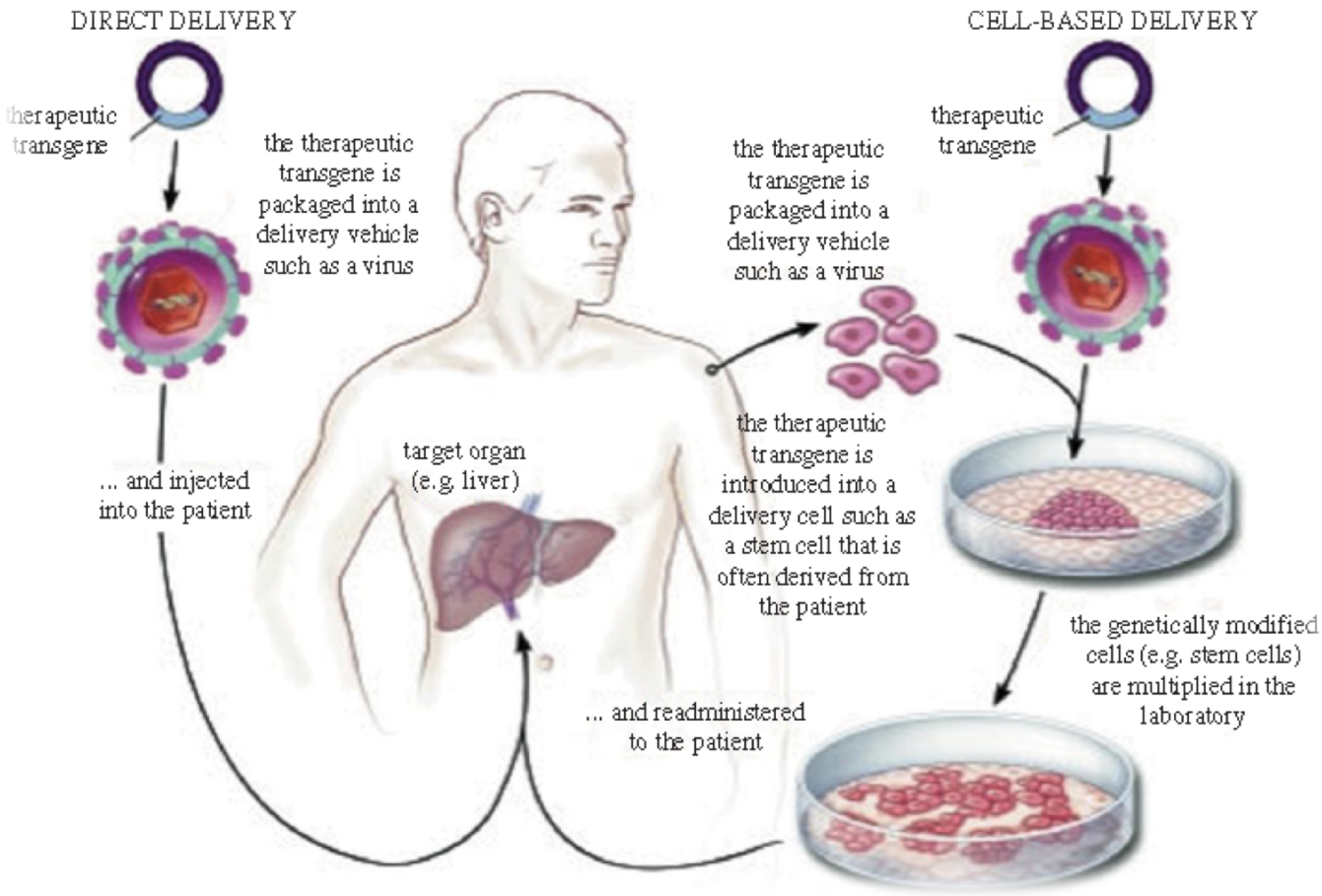


Not just a few base pairs!

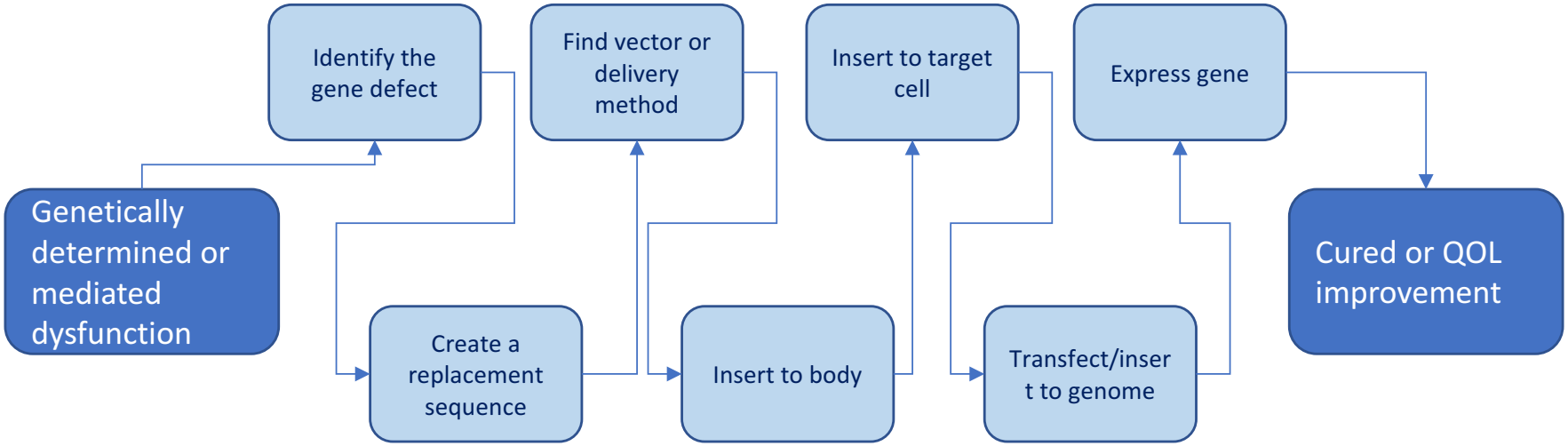
Insert to body step

In vivo

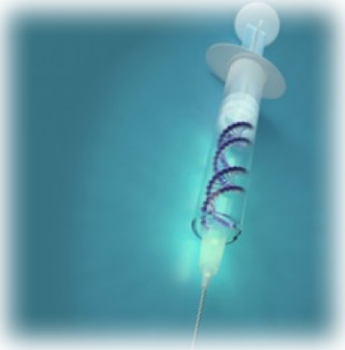
Ex vivo



Even seven steps is a simplification



Each step has many options and creates many challenges.
Advanced therapies really need new paradigm – especially when it comes to commercialisation models.



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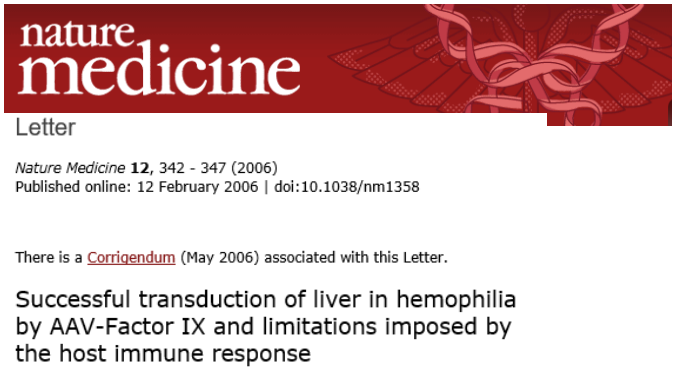
Pitfalls and setbacks

1999

2006



2008

2017

But…

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BIOTECH

Bluebird Bio's gene therapy for blood disorders yields some impressive results — but also raises questions

By ADAM FEUERSTEIN @adamfeuerstein / JUNE 23, 2017

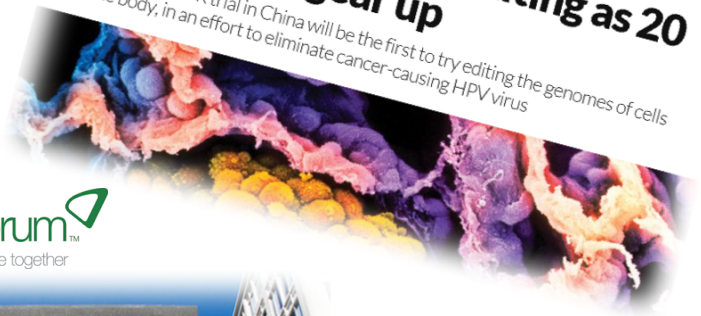
New Scientist

277

NEWS & TECHNOLOGY 30 May 2017, updated 7 June 2017

Boom in human gene editing as 20 CRISPR trials gear up

A pioneering CRISPR trial in China will be the first to try editing the genomes of cells inside the body, in an effort to eliminate cancer-causing HPV virus



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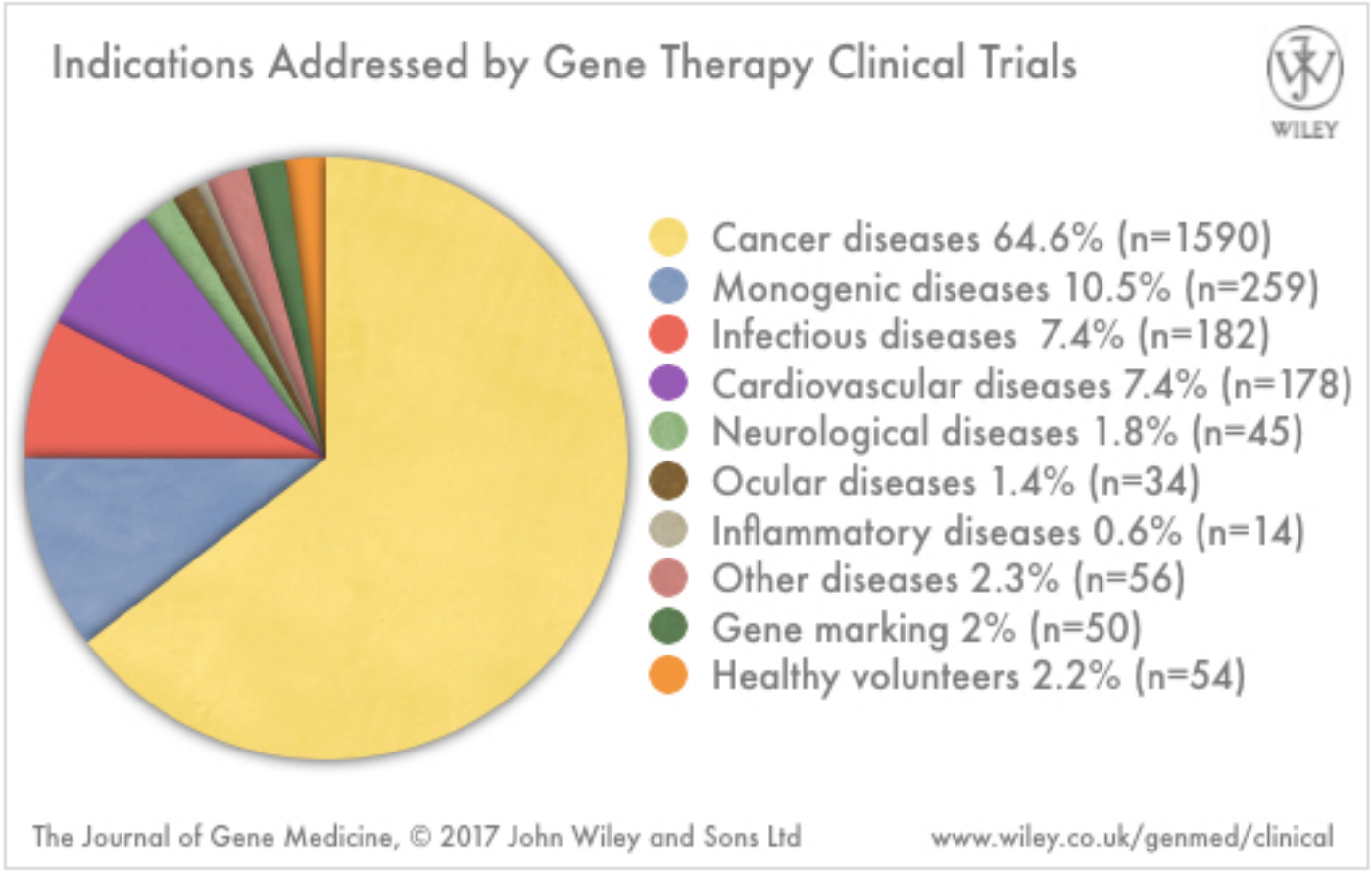
BRIEF

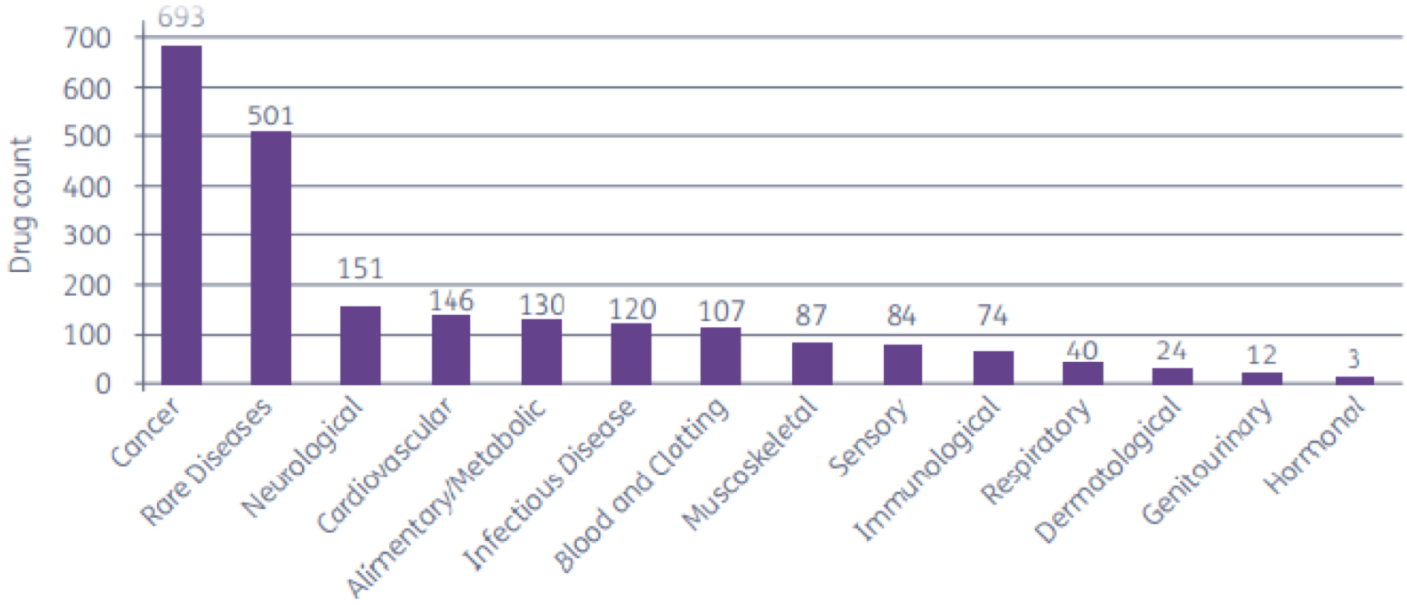
First gene therapy could hit the market in January

New 3-year data supports Kite 'cure' hopes for CAR-T

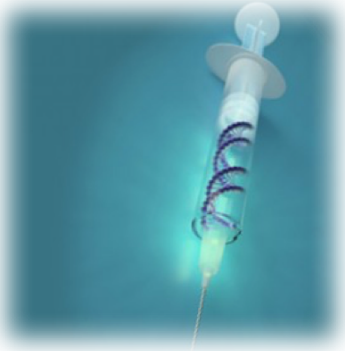
GT CTs by Clinical area



Number of GT drugs by TA



Source: Pharmaprojects, 2016



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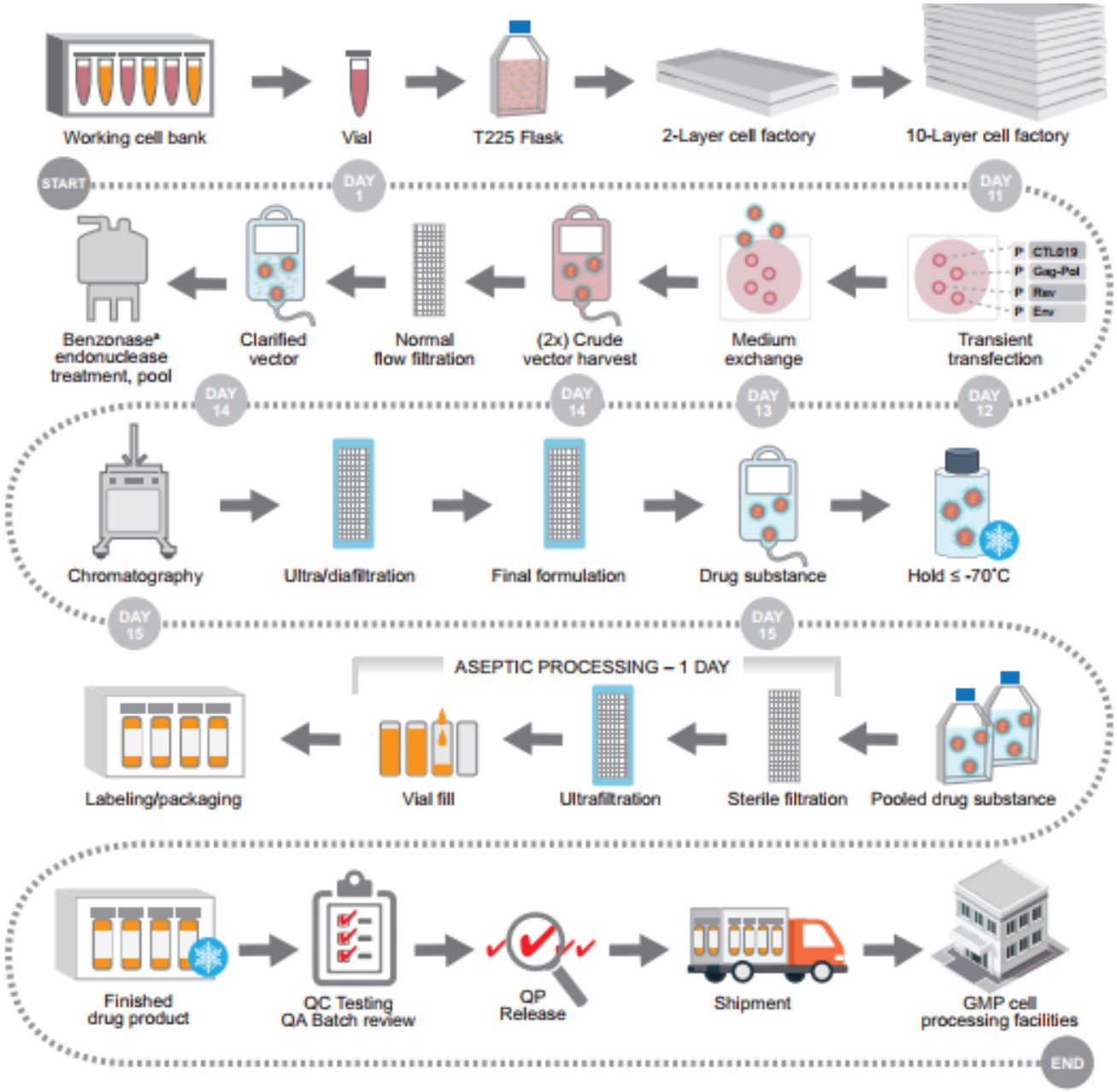
Challenges

Technical	Immunogenicity of vectors Off-target effects Non-vector delivery methods Base pairing restrictions (for editing) Sequence size restrictions (i.e. 5Kb in AAV) Scale up and scale out
Commercial	Manufacturing scalability and supply chain Regulatory needs, outcomes and measures Evidence generation Ethical dilemmas Value assessment and pricing modelling Affordability and equity Supply chain

Lentiviral vector manufacture



http://www.cell.com/molecular-therapy-family/methods/pdf/S2329-0501(16)30202-9.pdf

Biggest challenge – paying for it!

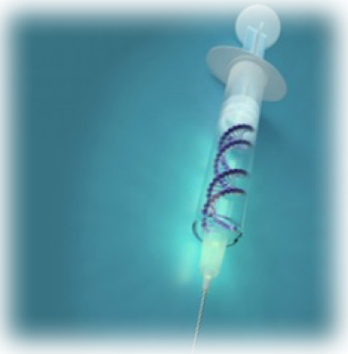
Only with collaborative efforts can the opportunities presented by GT be realised while addressing the significant challenges related to:

- *Evidence generation*
- *Value assessment*
- *Affordability*

Developer payer conversation

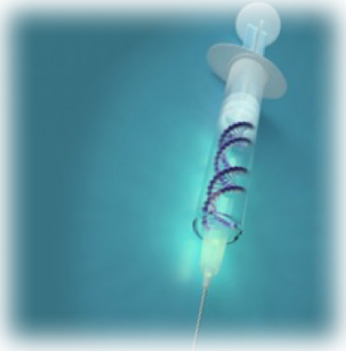
Agree	patient centred outcomes and drivers of value
Collaborate	on robustness of registration studies (often not RCT)
Partner	on post-approval studies, PVG, RWE generation etc.
Match	trial eligibility criteria to payment coverage measures
Agree	criteria for designation of COE (therapy delivery centres)
Explore	potential patient population size
Determine	place for the new therapy in the care pathway

https://icer-review.org/wp-content/uploads/2017/03/ICER-Gene-Therapy-White-Paper-030317.pdf



Opportunities – across sector

- Pre-competitive collaboration (e.g. scalability issues, vector agnostic development)
- Focused technical support to tackle specific technical issues
- Brokerage of the payer and developer dialogue
- Raise awareness of broader societal questions and issues with the specialist developers
- Leverage multi-therapy area patient groups like Genetic Alliance and other rare disease advocates
- Improved patient engagement across the sector



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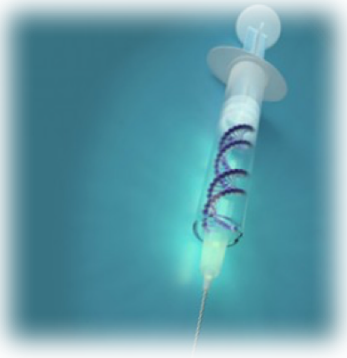

Opportunities for medcomms

- Pre-competitive collaboration awareness and support (novel client partnerships)
- Be sympathetic to the new value chain complexities
- Help to brokerage the payer and developer dialogue – with creative ideas
- Encourage multi-disciplinary advisory boards
- Publications will be wider and potentially more varied
- Learn from rare diseases but understand larger scale TA's will be much more challenging
- Support post-approval data generation and communication

Embrace wide collaboration

STEM CELLS TRANSLATIONAL MEDICINE

CANCER STEM CELLS

Concise Review: The High Cost of High Tech Medicine: Planning Ahead for Market Access

DAWN DRISCOLL,[a] STEPHANIE FARNIA,[b] PANOS KEFALAS,[c] RICHARD T. MAZIARZ[d]

Key Words. Acute myelogenous leukemia • Autologous stem cell transplantation • Hematopoietic stem cell transplantation • Cellular therapy

[a]DCi Biotech Inc. and DCi Biotech Pty Ltd., Perth, Australia; [b]American Society for Blood and Marrow Transplantation, Arlington Heights, Illinois, USA; [c]Cell and Gene Therapy Catapult Limited, London, United Kingdom; [d]Knight Cancer Institute, Oregon Health and Science University, Portland, Oregon, USA

ABSTRACT

Cellular therapies and other regenerative medicines are emerging as potentially transformative additions to modern medicine, but likely at a staggering financial cost. Public health care systems' budgets are already strained by growing and aging populations, and many private insurer's budgets are equally stretched. The current systems that most payers employ to manage their cash flow are not structured to absorb a sudden onslaught of very expensive prescriptions for a large portion of their covered population. Despite this, developers of new regenerative medicines tend to focus on the demands of regulators, not payers, in order to be compliant throughout the clinical trials phases, and to develop a product that ultimately will be approvable. It is not advisable to assume that an approved product will automatically become a reimbursed product, as examples from current practice in hematopoietic stem cell transplantation in the U.S. demonstrate; similarly, in Europe numerous Advanced-therapy Medicinal Products achieved market authorization but failed to secure reimbursement (e.g., Glybera, Provenge, ChondroCelect, MACI). There are however strat-

In this case industry, academia and governmental authors

Ideas for novel payment

Financials

How to cover Novartis' $475K CAR-T drug Kymriah? A 'new payment model' is the only way, Express Scripts says

by *Arlene Weintraub* | Sep 22, 2017 11:30am

Refs/sources and further reading

ICER Gene therapy report – Dec 2016
https://icer-review.org/wp-content/uploads/2017/03/ICER-Gene-Therapy-White-Paper-030317.pdf

Progresses towards safe and efficient gene therapy vectors
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4741561/pdf/oncotarget-06-30675.pdf

Gene Therapy: progress and predictions
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4707739/

Cell and Gene therapy Catapult papers
https://ct.catapult.org.uk/resources/publications/scientific-publications/all

Gene Therapies for Cancer: Strategies, Challenges and Successes
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4363073/

STATE-OF-THE-ART HUMAN GENE THERAPY: PART II. GENE THERAPY STRATEGIES AND APPLICATIONS
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4440458/pdf/nihms688231.pdf

Astrocyte Consulting

Thank you

Tim.Mustill@astrocyte.co.uk